relatively early. Many laboratories investigations and clinical reports of series of infections treated with the penicillin/streptomycin combination appeared to document the favorable response of patients to the combination.

Subsequent carefully controlled studies, increased insight into the importance of mixed bacterial flora and the significance in these infections of individual components of that flora, as well as the advances in chemotherapy with the discovery of new antibiotics have all operated to alter appreciably the logic behind this particular antibiotic combination.

The next portent of things to come and the initial departure from sound principles of chemotherapy appeared under the advocacy of Dr. Henry Welch, then Director of the Division of Antibiotics of the Food and Drug Administration. This was first documented in his opening remarks at the Fourth Symposium on Antibiotics and later published in Antibiotics Annual. By this time over 20 antibiotic agents had been described indicating this would be a fertile field for the discovery of agents beneficial in the treatment of disease. Already the ingenuity of the clinical investigators as well as the pharmaceutical industry was stimulated by speculation concerning the effect of various antibiotic combinations, particularly in connection with the agents in which they were individually involved. Dr. Welch specifically mentioned twelve combinations of antibiotics, a number of which fortunately have never found their way to the market place. No allusion was made to fixed combinations of antibiotics but these had already appeared and received the tacit approval of the Food and Drug Administration.

Mr. GORDON. Dr. Hewitt, is it true that Dr. Welch was the FDA official responsible for the approval of the marketing of these fixed combinations?

Dr. HEWITT. I think that at this time Dr. Welch's title was director of the division of antibiotics of the FDA. I don't think he was the administrator, but I think he was the one that was responsible for the approval of such—or at least let's say certifying—I would presume as to their safety.

Mr. GORDON. His activities had something to do with popularizing them too.

Dr. HEWITT. Oh, yes. His opening statements at this particular meeting were very dramatic ones. And it was immediately recognized by all the clinical investigators and medical people present at this meeting that this was a distinct policy which was now being promulgated. And at this time it was recognized by him, if not the majority of the people, that it was a very had policy.

Senator NELSON. When was this?

Dr. HEWITT. The reference is given here, 1956.

This concept was further supported by the statement that there was "a distinct trend toward combined therapy, not an old fashioned 'shotgun' approach, but a calculated rational method of attacking the problem of resistant organisms." Despite this statement it was clear to many that the commonest purpose for the fixed combinations which were appearing was precisely that it was claimed not to be; namely, a shotgun approach to the treatment of undiagnosed disease. This was defined as a third era of antibiotic therapy, one in which combined